

Supplementary online content

Appendix 1. Search terms

Suppl. Figure 1. Flow diagram of study retrieval for the systematic review.

Suppl. Figure 2. Publication and related biases assessment: Doi plot of the prevalence of ultimate local failure in all the patients starting radio(chemo)therapy as potential candidates for watch-and-wait.

Suppl. Figure 3. Publication and related biases assessment: Doi plot of the prevalence of ultimate local failure in the patients starting watch-and-wait.

Suppl. Figure 4. Publication and related biases assessment: Doi plot of the prevalence of ultimate local failure in the patients with regrowth.

Suppl. Figure 5. The pooled weighted rate of patients refusing salvage surgery among those with regrowth.

Suppl. Figure 6. The pooled weighted rate of patients with ultimate local failure because of recurrence after salvage TME among those with regrowth.

Suppl. Figure 7. The pooled weighted rate of patients with ultimate local failure because of simultaneous distant metastases among those with regrowth.

Suppl. Figure 8. The pooled weighted rate of patients with ultimate local failure because of unresectable pelvic disease among those with regrowth.

Suppl. Figure 9. The pooled weighted rate of patients with ultimate local failure because of frailty among those with regrowth.

Suppl. Figure 10. The pooled weighted rate of patients with ultimate local failure because of other reasons among those with regrowth.

Suppl. Figure 11. The pooled weighted rate of patients refusing salvage surgery among those with persistent tumour.

Suppl. Table 1. The modified Newcastle-Ottawa scale (NOS) used for study quality assessment.

Suppl. Table 2. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) checklist.

Suppl. Table 3. Sensitivity analysis: Ultimate local failure in all the patients starting radio(chemo)therapy as potential candidates for watch-and-wait.

Suppl. Table 4. Sensitivity analysis: Ultimate local failure in the patients starting watch-and-wait.

Suppl. Table 5. Sensitivity analysis: Ultimate local failure in the patients with regrowth.

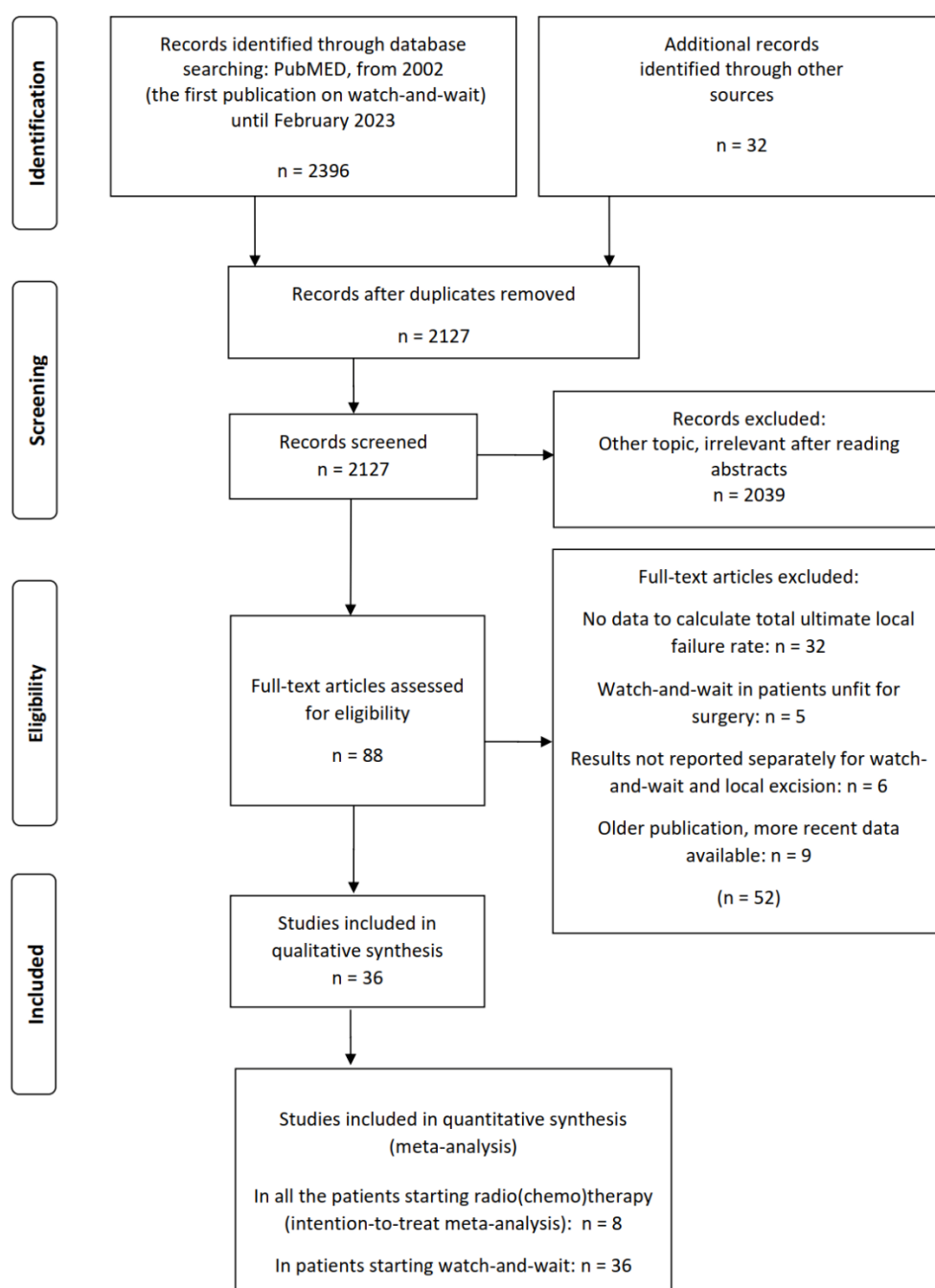
Abbreviations:

TME – total mesorectal excision, TNT – total neoadjuvant therapy, RT – radiotherapy, w&w – watch-and-wait, NAN – Not-A-Number

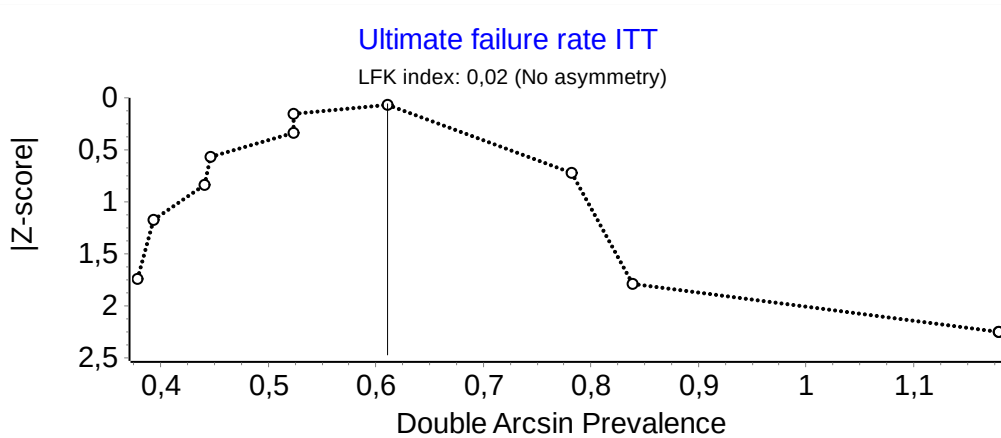
Appendix 1. Search terms.

((("rectal neoplasms"[MeSH Terms] OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR "rectal neoplasms"[All Fields] OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "rectal cancer"[All Fields] OR ("administration, rectal"[MeSH Terms] OR ("administration"[All Fields] AND "rectal"[All Fields]) OR "rectal administration"[All Fields] OR "rectal"[All Fields]) AND ("adenocarcinoma"[MeSH Terms] OR "adenocarcinoma"[All Fields] OR "adenocarcinomas"[All Fields] OR "adenocarcinoma s"[All Fields])))) AND "non-operative"[All Fields]) OR "watch-and-wait"[All Fields] OR "organ-preserving"[All Fields]).

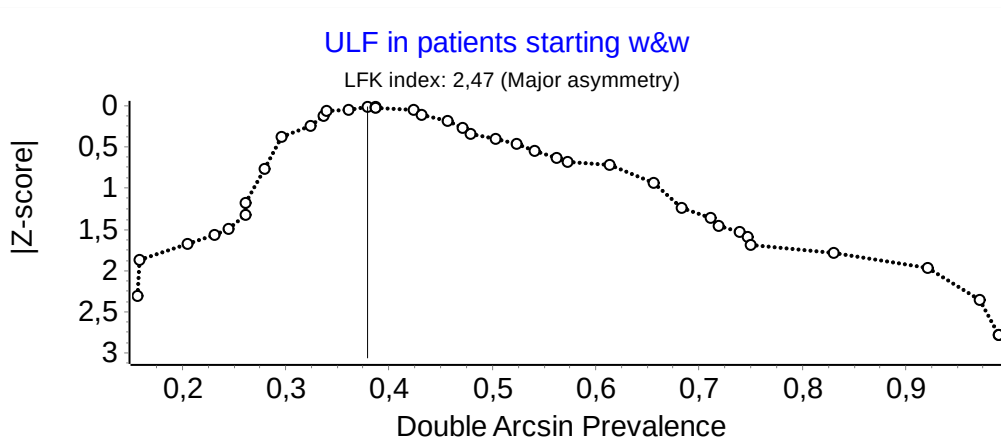
Suppl. Figure 1. Flow diagram of study retrieval for the systematic review.



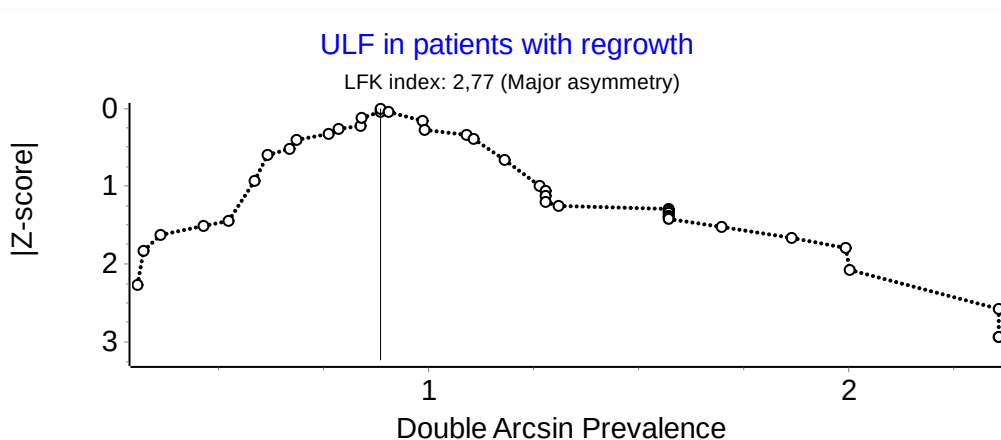
Suppl. Figure 2. Publication and related biases assessment: Doi plot of the prevalence of ultimate local failure in all the patients starting radio(chemo)therapy as potential candidates for watch-and-wait.



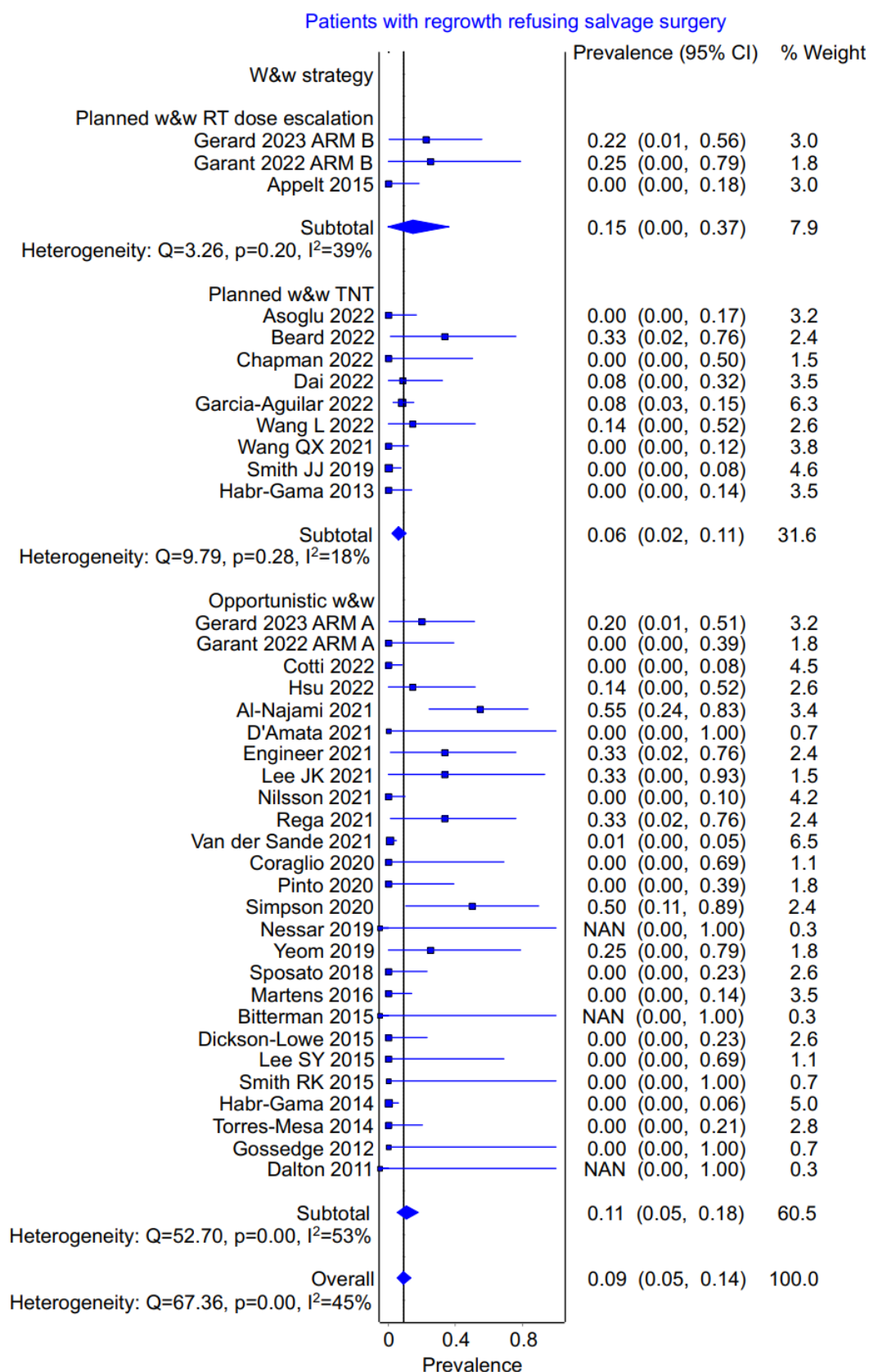
Suppl. Figure 3. Publication and related biases assessment: Doi plot of the prevalence of ultimate local failure in the patients starting watch-and-wait.



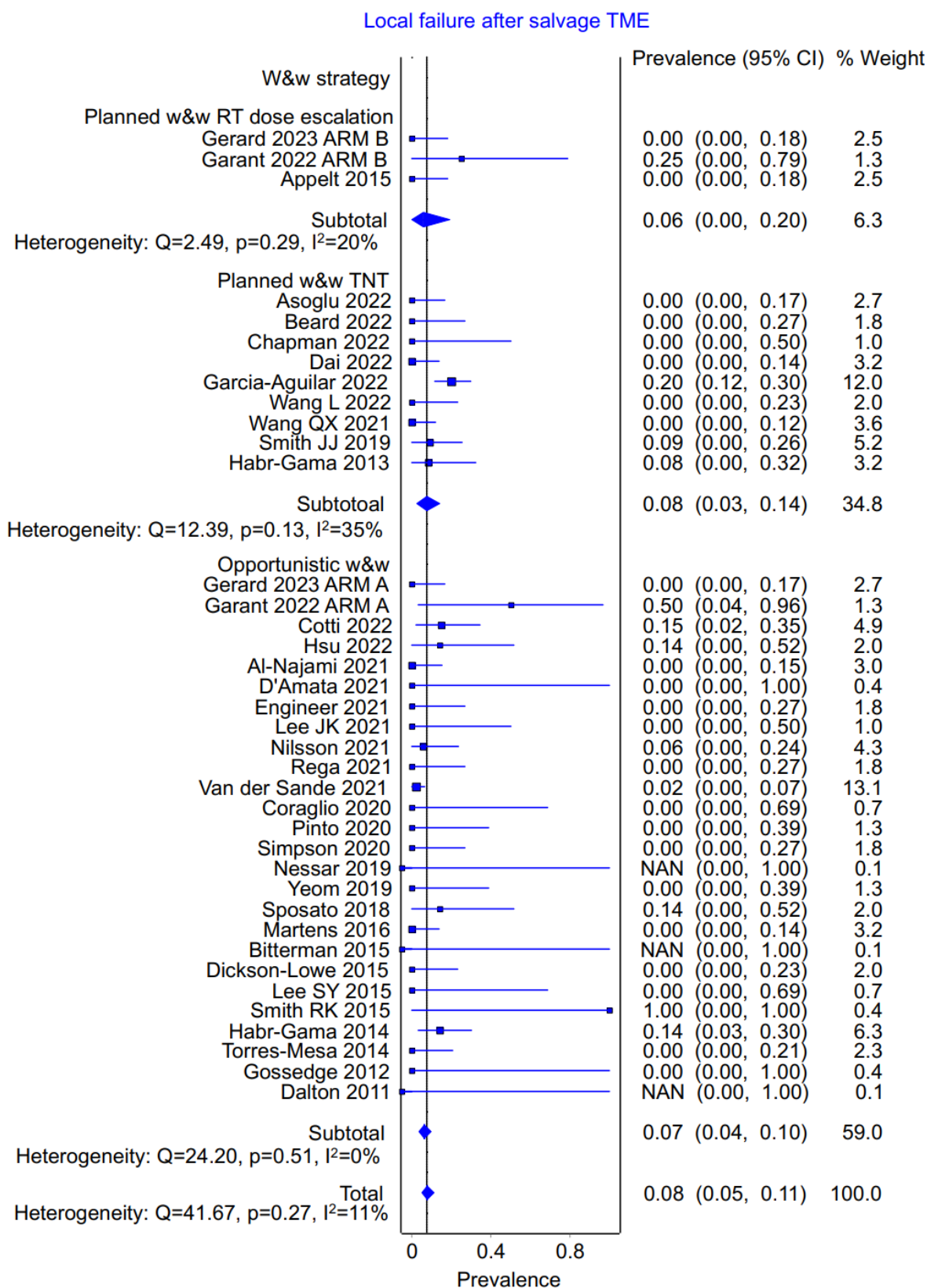
Suppl. Figure 4. Publication and related biases assessment: Doi plot of the prevalence of ultimate local failure in the patients with regrowth.



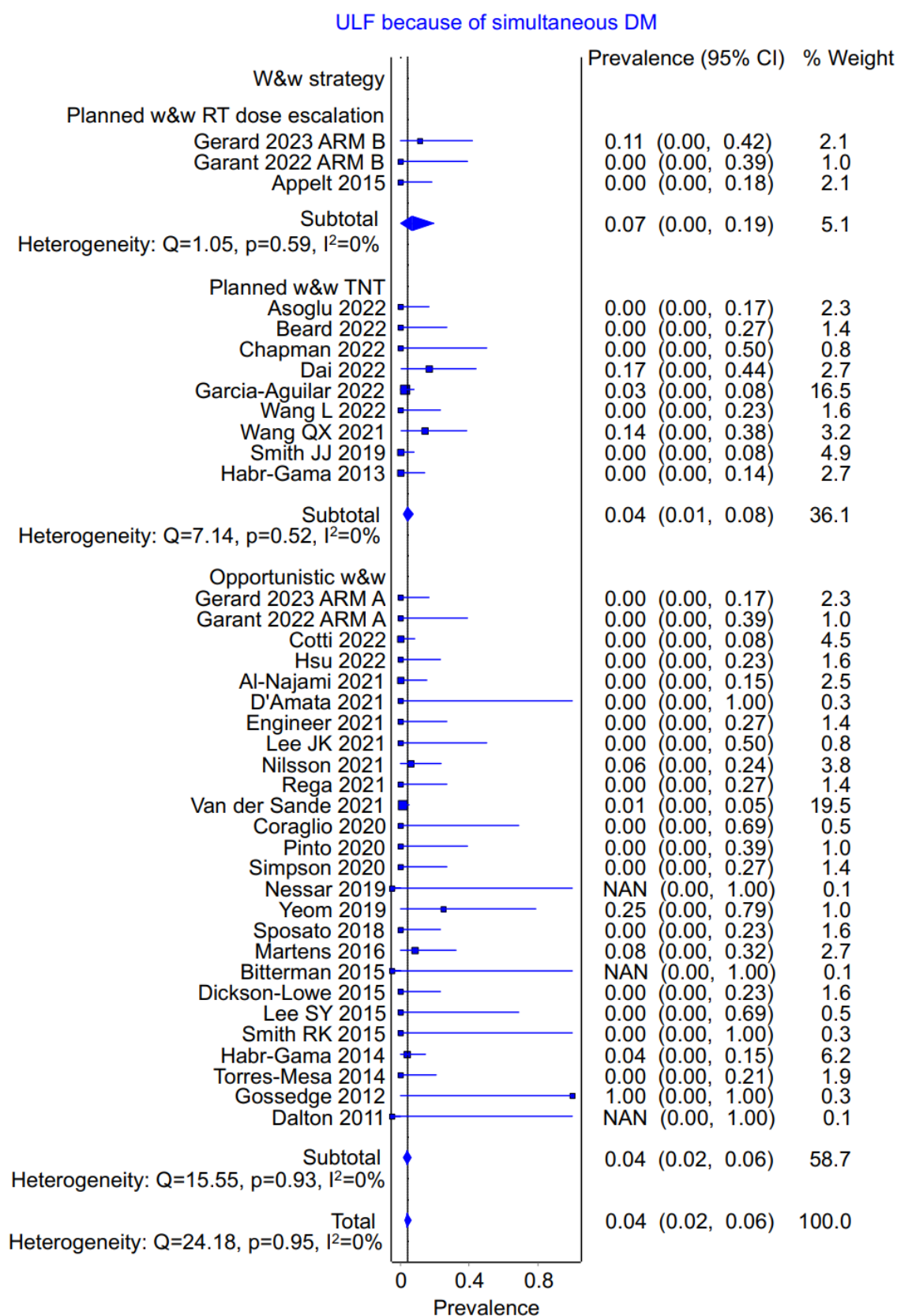
Suppl. Fig. 5. The pooled weighted rate of patients refusing salvage surgery among those with regrowth.



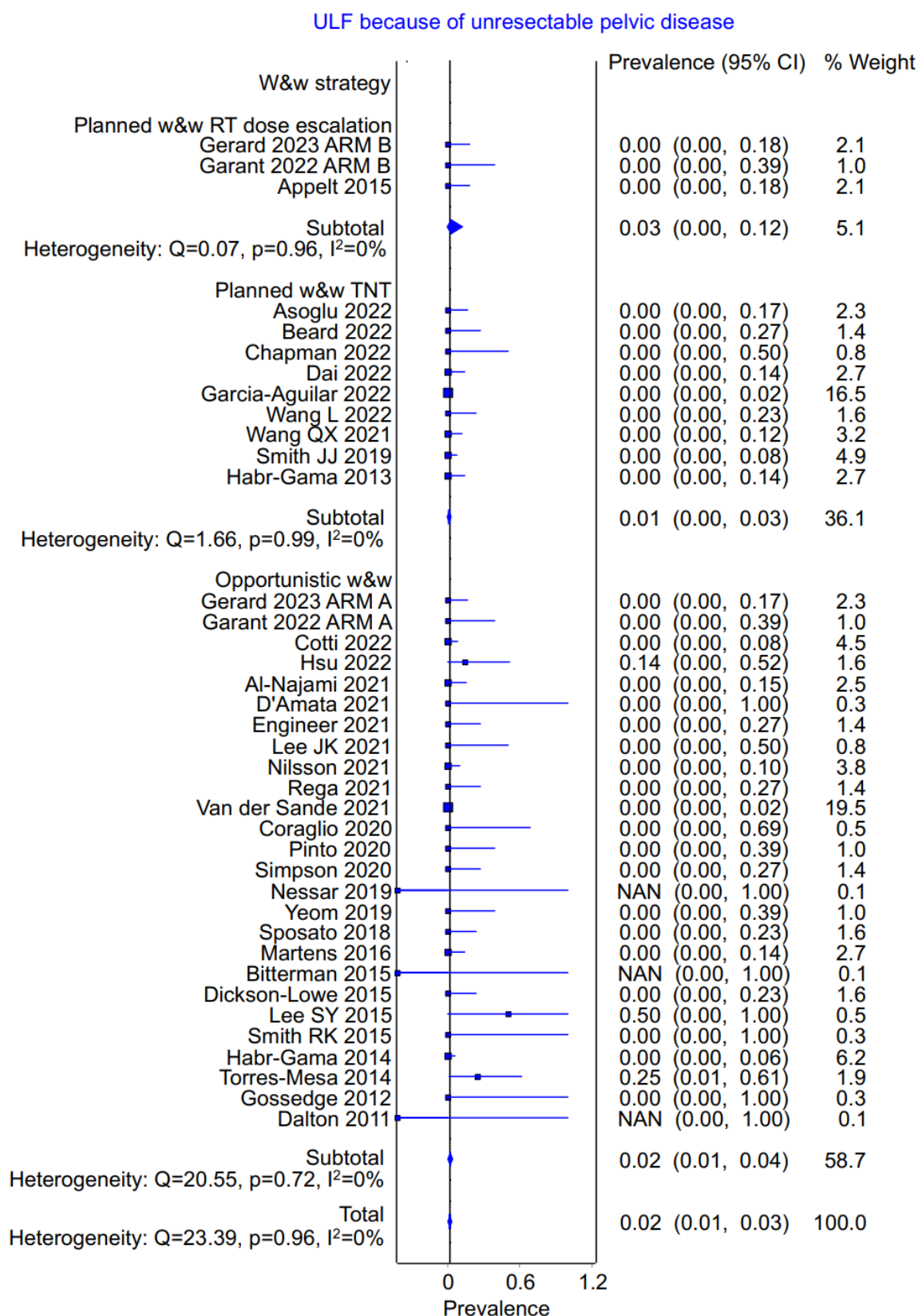
Suppl. Fig. 6. The pooled weighted rate of patients with ultimate local failure because of recurrence after salvage TME among those with regrowth.



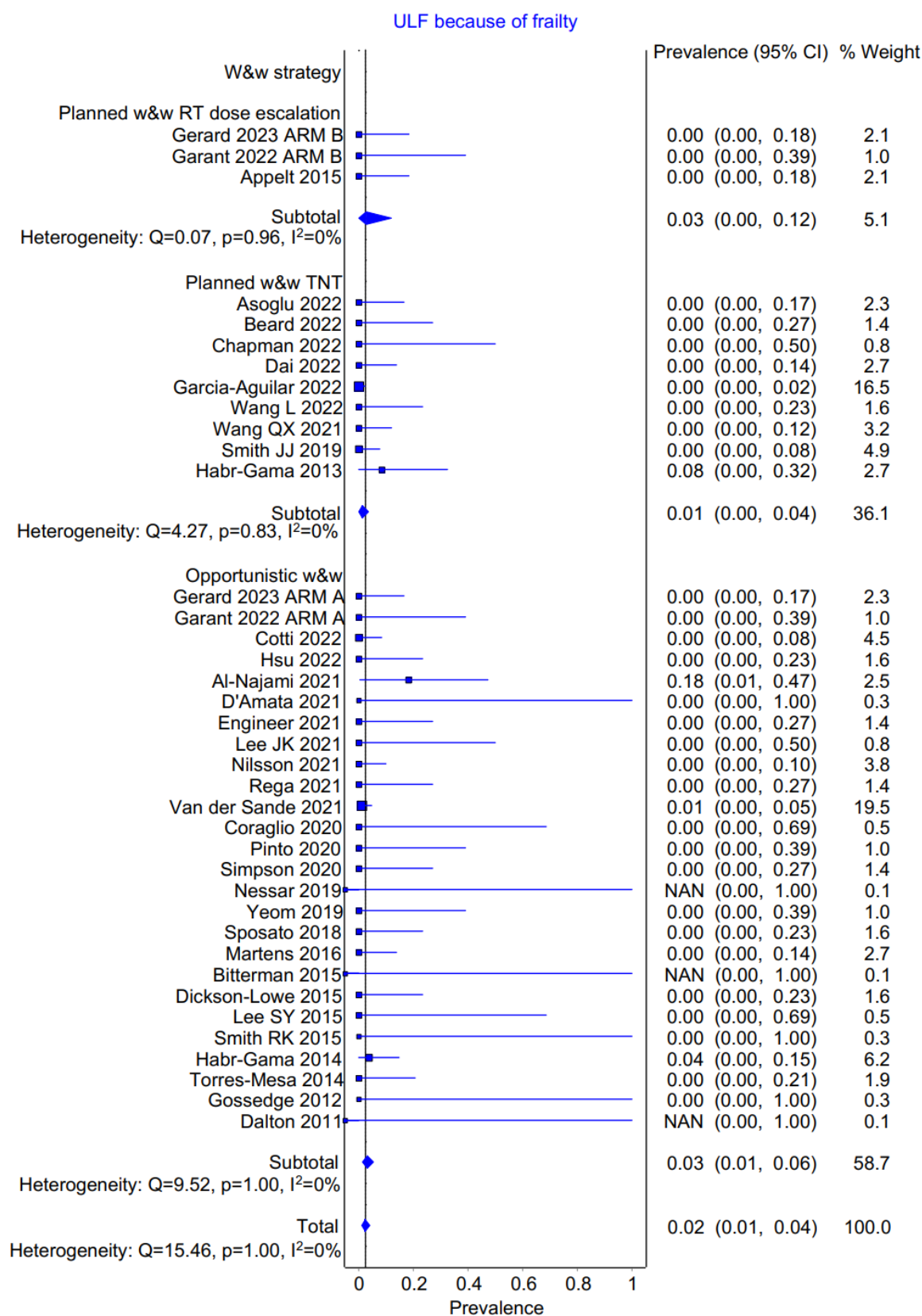
Suppl. Fig. 7. The pooled weighted rate of patients with ultimate local failure because of simultaneous distant metastases among those with regrowth.



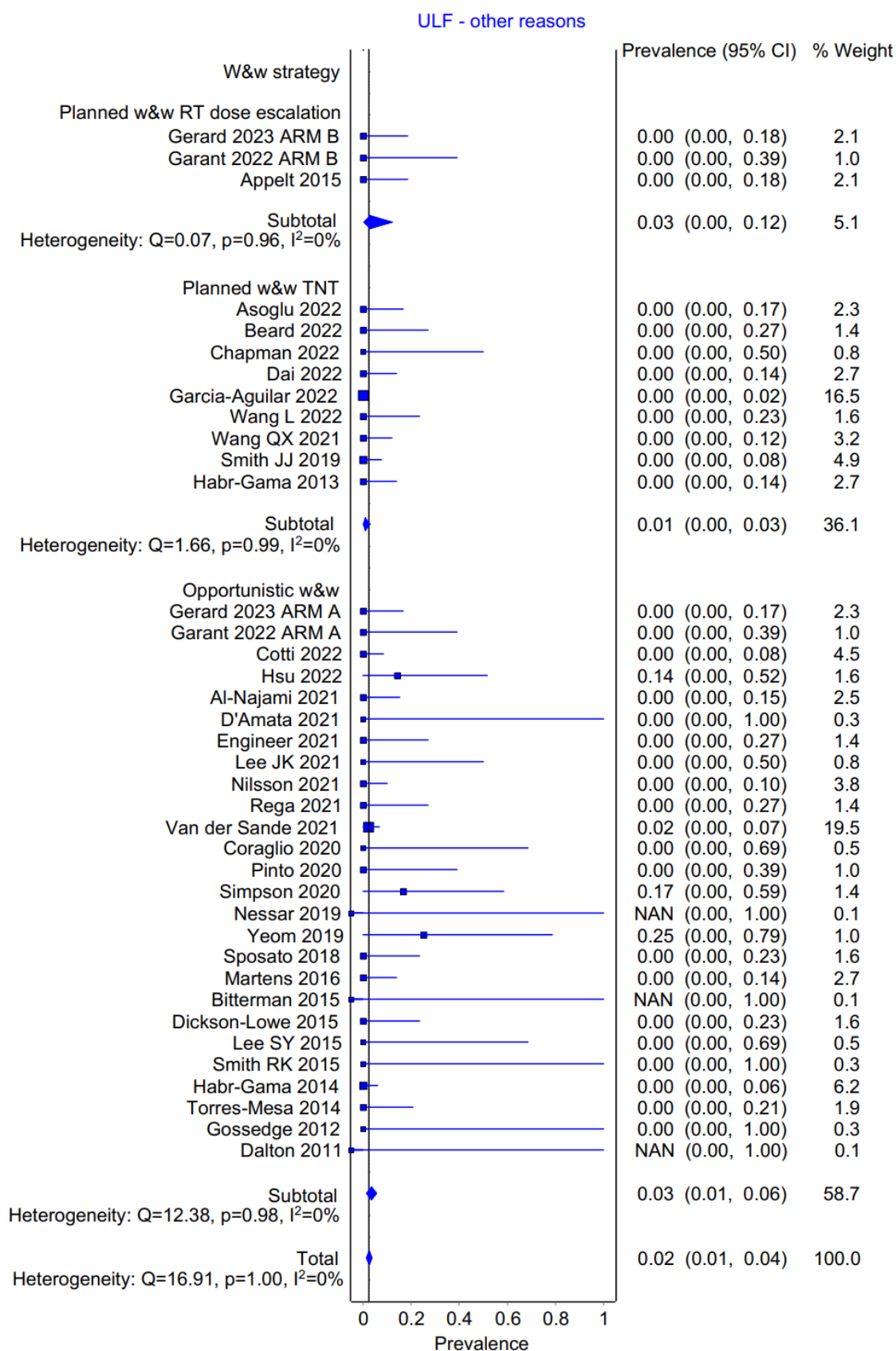
Suppl. Fig. 8. The pooled weighted rate of patients with ultimate local failure because of unresectable pelvic disease among those with regrowth.



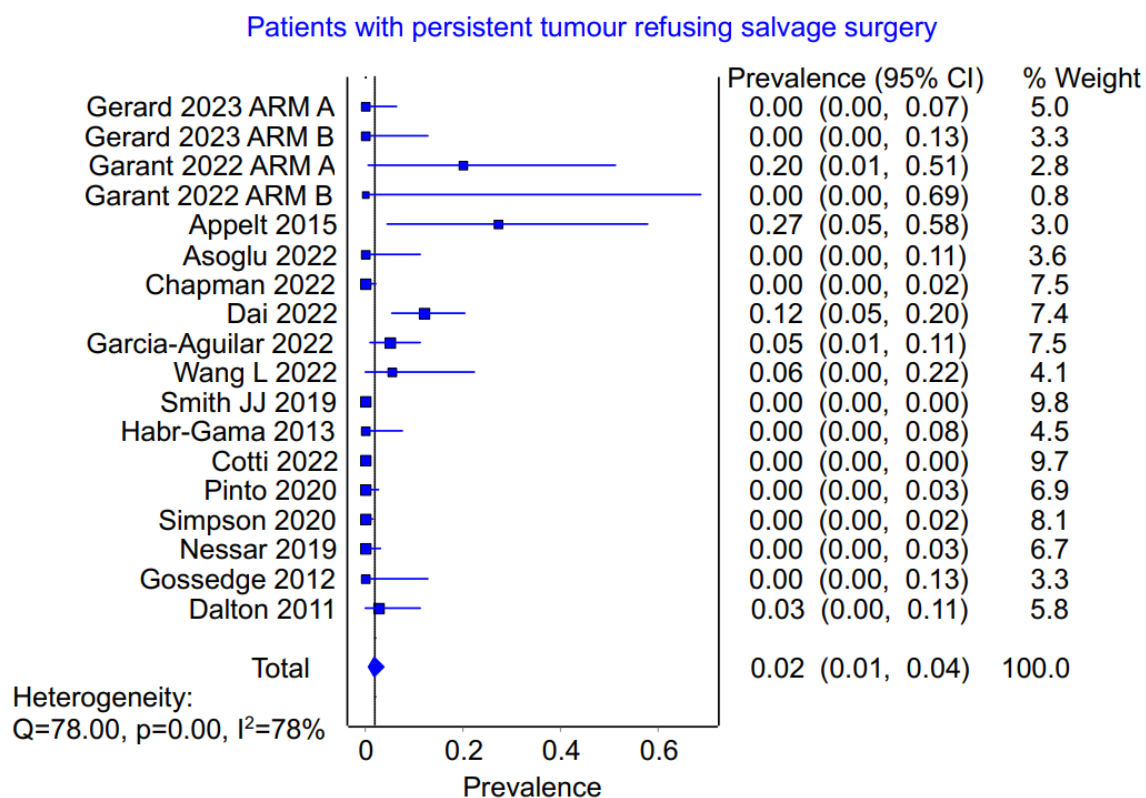
Suppl. Fig. 9. The pooled weighted rate of patients with ultimate local failure because of frailty among those with regrowth.



Suppl. Fig. 10. The pooled weighted rate of patients with ultimate local failure because of other reasons among those with regrowth.



Suppl. Fig. 11. The pooled weighted rate of patients refusing salvage surgery among those with persistent tumour.



Supplementary Table 1. The modified Newcastle-Ottawa scale (NOS) used for study quality assessment

Study	Selection (score)				Comparability (score)	Outcome (score)		
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest not present at start of study	Control of cohorts on the basis of the design or analysis	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts
Appelt 2015	*	NA	*	*	NA	*	0	*
Asoglu 2022	*	NA	*	*	NA	*	*	*
Wang L 2022	*	NA	*	*	NA	*	*	*
Pinto 2020	*	NA	*	*	NA	*	0	*
Habr-Gama 2013	*	NA	*	*	NA	*	0	*
Beard 2022	*	NA	*	*	NA	*	0	*
Chapman 2022	*	NA	*	*	NA	*	0	*
Dai 2022	*	NA	*	*	NA	*	0	*
Wang QX 2021	*	NA	*	*	NA	*	*	*
Smith JJ 2019	*	NA	*	*	NA	*	0	*
Cotti 2022	*	NA	*	*	NA	*	*	*
Hsu 2022	*	NA	*	*	NA	*	*	*
Al-Najami 2021	*	NA	*	*	NA	*	*	*
D'Amata 2021	*	NA	*	*	NA	*	0	*
Engineer 2021	*	NA	*	*	NA	*	0	*
Lee JK 2021	*	NA	*	*	NA	*	*	*
Nilsson 2021	*	NA	*	*	NA	*	0	*
Rega 2021	*	NA	*	*	NA	*	0	*
Van der Sande 2021	*	NA	*	*	NA	*	0	*
Coraglio 2020	*	NA	*	*	NA	*	*	*
Simpson 2020	*	NA	*	*	NA	*	*	*
Nessar 2019	*	NA	*	*	NA	*	*	*
Yeom 2019	*	NA	*	*	NA	*	0	*
Sposato 2018	*	NA	*	*	NA	*	*	*
Martens 2016	*	NA	*	*	NA	*	*	*
Bitterman 2015	*	NA	*	*	NA	*	0	*
Dickson-Lowe 2015	*	NA	*	*	NA	*	0	*
Lee SY 2015	*	NA	*	*	NA	*	*	*
Smith RK 2015	*	NA	*	*	NA	*	*	*
Habr-Gama 2014	*	NA	*	*	NA	*	*	*
Torres-Mesa 2014	*	NA	*	*	NA	*	0	*
Gossedge 2012	*	NA	*	*	NA	*	*	*
Dalton 2011	*	NA	*	*	NA	*	0	*

Not applicable: our study is not a comparative analysis.

Supplementary Table 2. MOOSE checklist.

Section/topic	Checklist item	Reported on page #
Reporting of background	Problem definition	2–3
	Hypothesis statement	2–3
	Description of study outcome(s)	3
	Type of exposure or intervention used	3
	Type of study designs used	3
	Study population	3–4
Reporting of search strategy	Qualifications of searches (eg, librarians and investigators)	4
	Search strategy, including time period included in the synthesis and key words	4
	Effort to include all available studies, including contact with authors	4
	Databases and registries searched	4
	Search software used, name and version, including special issues used	4
	Use of hand searching (eg, reference lists of obtained articles)	4
	List of citations located and those excluded, including justification	4
	Method of addressing articles published in languages other than English	4
	Method of handling abstracts and unpublished articles	4
	Description of any contact with authors	4
Reporting of methods	Description of relevance and appropriateness of studies assembled for assessing the hypothesis to be tested	4
	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	4
	Documentation of how data were classified and coded (eg, multiple raters, blinding, and inter-rater reliability)	4
	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	4
	Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	4
	Assessment of heterogeneity	4
	Description of statistical methods (eg, complete description of fixed or random effect models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient details to be replicated	4–5
	Provision of appropriate tables and graphics	4–5
Reporting of results	Graphic summarizing individual study estimates and overall estimate	5
	Table giving descriptive information for each study included	19–27
	Results of sensitivity testing (eg, subgroup analysis)	6
	Indication of statistical uncertainty of findings	6
Reporting of discussion	Quantitative assessment of bias (eg, publication bias)	6
	Justification for exclusion (eg, exclusion of non-English-language citations)	4
	Assessment of quality of included studies	4, suppl.
Reporting of conclusions	Considerations of alternative explanations for observed results	7–10
	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	7–10
	Guidelines for future research	10
	Disclosure of founding source	title page

Supplementary Table 3. Sensitivity analysis: Ultimate local failure in all the patients starting radio(chemo)therapy as potential candidates for watch-and-wait.

Excluded study	Pooled Prevalence	LCI 95%	HCI 95%	Cochran Q	p	I 2	I 2 LCI 95%	I 2 HCI 95%
Gerard 2023 ARM A	0,087	0,052	0,130	24,252	0,002	67,013	33,364	83,670
Gerard 2023 ARM B	0,085	0,049	0,129	26,094	0,001	69,342	38,787	84,645
Garant 2022 ARM A	0,071	0,042	0,106	21,939	0,005	63,535	25,179	82,228
Garant 2022 ARM B	0,076	0,043	0,117	27,543	0,001	70,954	42,508	85,325
Garcia-Aguilar 2022	0,069	0,041	0,103	15,048	0,058	46,836	0,000	75,328
Asoglu 2022	0,082	0,046	0,127	27,942	0,000	71,369	43,462	85,501
Wang 2022	0,086	0,051	0,130	25,057	0,002	68,073	35,839	84,113
Pinto 2020	0,079	0,043	0,126	28,572	0,000	72,001	44,909	85,770
Appelt 2015	0,082	0,046	0,127	28,095	0,000	71,525	43,820	85,568
Habr-Gama 2013	0,085	0,049	0,129	26,336	0,001	69,624	39,440	84,764

Supplementary Table 4. Sensitivity analysis: Ultimate local failure in the patients starting watch-and-wait.

Excluded study	Pooled Prevalence	LCI 95%	HCI 95%	Cochran Q	p	I 2	I 2 LCI 95%	I 2 HCI 95%
Gerard 2023 ARM A	0,053	0,038	0,071	70,218	0,001	48,731	24,851	65,022
Gerard 2023 ARM B	0,054	0,039	0,072	70,705	0,000	49,084	25,415	65,242
Garant 2022 ARM A	0,052	0,038	0,069	67,574	0,001	46,725	21,644	63,777
Garant 2022 ARM B	0,053	0,038	0,070	69,096	0,001	47,899	23,522	64,506
Appelt 2015	0,056	0,041	0,073	67,451	0,001	46,628	21,490	63,717
Asoglu 2022	0,056	0,041	0,073	67,580	0,001	46,729	21,652	63,780
Beard 2022	0,054	0,039	0,072	70,764	0,000	49,126	25,483	65,268
Chapman 2022	0,055	0,040	0,072	69,956	0,001	48,539	24,545	64,903
Dai 2022	0,052	0,038	0,069	68,289	0,001	47,283	22,538	64,124
Garcia-Aguilar 2022	0,050	0,036	0,067	58,783	0,010	38,758	8,849	58,852
Wang L 2022	0,055	0,039	0,072	70,616	0,000	49,020	25,313	65,202
Wang QX 2021	0,055	0,040	0,073	69,438	0,001	48,155	23,931	64,665
Smith JJ 2019	0,056	0,040	0,074	68,261	0,001	47,261	22,503	64,110
Habr-Gama 2013	0,054	0,039	0,071	70,700	0,000	49,080	25,409	65,239
Cotti 2022	0,054	0,039	0,072	70,748	0,000	49,115	25,465	65,261
Hsu 2022	0,052	0,037	0,069	68,025	0,001	47,078	22,210	63,997
Al-Najami 2021	0,050	0,036	0,066	60,706	0,006	40,697	11,970	60,050
D'Amata 2021	0,054	0,039	0,071	70,682	0,000	49,068	25,389	65,232
Engineer 2021	0,054	0,038	0,071	70,509	0,001	48,942	25,189	65,154
Lee JK 2021	0,053	0,038	0,070	69,774	0,001	48,405	24,330	64,820
Nilsson 2021	0,055	0,040	0,073	69,797	0,001	48,422	24,358	64,830
Rega 2021	0,054	0,038	0,071	70,608	0,000	49,014	25,303	65,198
Van der Sande 2021	0,056	0,041	0,073	58,377	0,011	38,331	8,163	58,589
Coraglio 2020	0,055	0,040	0,073	69,461	0,001	48,172	23,959	64,675
Pinto 2020	0,055	0,039	0,072	70,135	0,001	48,670	24,755	64,985
Simpson 2020	0,052	0,037	0,069	68,383	0,001	47,355	22,653	64,168
Nessar 2019	0,054	0,039	0,071	70,721	0,000	49,096	25,434	65,249
Yeom 2019	0,052	0,037	0,068	66,354	0,002	45,745	20,076	63,171
Sposato 2018	0,054	0,039	0,072	70,759	0,000	49,123	25,477	65,266
Martens 2016	0,056	0,040	0,074	67,907	0,001	46,986	22,063	63,940
Bitterman 2015	0,054	0,039	0,071	70,750	0,000	49,116	25,467	65,262
Dickson-Lowe 2015	0,055	0,039	0,072	70,300	0,001	48,791	24,948	65,060
Lee SY 2015	0,053	0,038	0,070	69,464	0,001	48,174	23,963	64,677
Smith RK 2015	0,053	0,038	0,071	70,490	0,001	48,929	25,167	65,145
Habr-Gama 2014	0,053	0,038	0,071	69,803	0,001	48,427	24,365	64,833
Torres-Mesa 2014	0,053	0,038	0,070	69,229	0,001	47,998	23,681	64,567
Gossedge 2012	0,053	0,038	0,071	70,294	0,001	48,786	24,940	65,057
Dalton 2011	0,054	0,039	0,071	70,750	0,000	49,116	25,467	65,262

Supplementary Table 5. Sensitivity analysis: Ultimate local failure in the patients with regrowth.

Excluded study	Pooled Prevalence	LCI 95%	HCI 95%	Cochran Q	p	I 2	I 2 LCI 95%	I 2 HCI 95%
Gerard 2023 ARM A	0,242	0,178	0,313	74,568	0,000	51,722	29,617	66,885
Gerard 2023 ARM B	0,238	0,175	0,308	73,628	0,000	51,106	28,637	66,500
Garant 2022 ARM A	0,236	0,174	0,305	72,835	0,000	50,573	27,789	66,169
Garant 2022 ARM B	0,236	0,174	0,305	72,835	0,000	50,573	27,789	66,169
Appelt 2015	0,250	0,187	0,319	70,753	0,000	49,119	25,471	65,263
Asoglu 2022	0,250	0,187	0,319	70,129	0,001	48,666	24,747	64,982
Beard 2022	0,239	0,175	0,308	73,879	0,000	51,271	28,900	66,604
Chapman 2022	0,245	0,181	0,314	73,943	0,000	51,314	28,968	66,630
Dai 2022	0,241	0,177	0,311	74,338	0,000	51,572	29,379	66,791
Garcia-Aguilar 2022	0,238	0,173	0,309	69,845	0,001	48,457	24,415	64,852
Wang L 2022	0,243	0,179	0,313	74,553	0,000	51,712	29,601	66,878
Wang QX 2021	0,245	0,180	0,316	74,395	0,000	51,609	29,438	66,814
Smith JJ 2019	0,249	0,184	0,320	72,711	0,000	50,489	27,655	66,116
Habr-Gama 2013	0,244	0,179	0,314	74,558	0,000	51,715	29,606	66,881
Cotti 2022	0,246	0,180	0,317	74,321	0,000	51,561	29,361	66,784
Hsu 2022	0,232	0,171	0,299	70,332	0,001	48,814	24,984	65,074
Al-Najami 2021	0,222	0,165	0,284	61,524	0,005	41,486	13,239	60,537
D'Amata 2021	0,242	0,179	0,311	74,544	0,000	51,707	29,592	66,875
Engineer 2021	0,239	0,175	0,308	73,879	0,000	51,271	28,900	66,604
Lee JK 2021	0,239	0,176	0,308	74,131	0,000	51,438	29,165	66,707
Nilsson 2021	0,247	0,182	0,318	73,929	0,000	51,305	28,953	66,624
Rega 2021	0,239	0,175	0,308	73,879	0,000	51,271	28,900	66,604
Van der Sande 2021	0,251	0,189	0,318	59,775	0,008	39,774	10,485	59,480
Coraglio 2020	0,244	0,180	0,313	74,304	0,000	51,550	29,344	66,777
Pinto 2020	0,246	0,182	0,315	73,509	0,000	51,027	28,511	66,451
Simpson 2020	0,231	0,170	0,297	69,081	0,001	47,887	23,504	64,499
Nessar 2019	0,241	0,178	0,309	74,393	0,000	51,608	29,436	66,814
Yeom 2019	0,232	0,171	0,298	69,642	0,001	48,307	24,174	64,759
Sposato 2018	0,243	0,179	0,313	74,553	0,000	51,712	29,601	66,878
Martens 2016	0,247	0,182	0,317	73,675	0,000	51,137	28,686	66,520
Bitterman 2015	0,241	0,178	0,309	74,393	0,000	51,608	29,436	66,814
Dickson-Lowe 2015	0,249	0,185	0,318	71,941	0,000	49,959	26,811	65,786
Lee SY 2015	0,238	0,176	0,307	73,617	0,000	51,099	28,625	66,496
Smith RK 2015	0,236	0,175	0,303	71,611	0,000	49,728	26,443	65,642
Habr-Gama 2014	0,243	0,178	0,315	74,547	0,000	51,708	29,595	66,876
Torres-Mesa 2014	0,240	0,177	0,310	74,374	0,000	51,596	29,417	66,806
Gossedge 2012	0,236	0,175	0,303	71,611	0,000	49,728	26,443	65,642
Dalton 2011	0,241	0,178	0,309	74,393	0,000	51,608	29,436	66,814